

Applicants: Ira Tabas
Serial No.: 10/767,749
Filed: January 28, 2004
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REMARKS

Claims 1, 2, 27, 50, 53, 62 and 65-70 are pending in the subject application. Claims 65-67 have been withdrawn as being drawn to a nonelected species. Applicant has hereinabove amended claims 1, 2 and 27. Support for the amendments to claims 1, 2 and 27 may be found, *inter alia*, in the specification as follows: page 100, lines 29-32. Applicant maintains that no issue of new matter is raised by these amendments. Upon entry of this Amendment, claims 1, 2, 27, as amended, and claims 50, 53, and 62 will be pending and under examination.

Information Disclosure Statement

Applicant notes that the Examiner has crossed off on the Form 1449 IDS filed August 23, 2007, several references that were cited in duplicate or were listed on the PTO-892 form mailed with the previous Office Action of February 13, 2007. Applicant agrees that the references crossed off either are duplicate listings of references which have been initialed or are listed on the PTO-892 form referenced by the Examiner. Accordingly, applicant understands resubmission of the crossed off references is not required.

Rejections under 35 U.S.C. §103

The Examiner rejected claims 1, 2, 27, 50, 53 and 62 under 35 U.S.C. §103(a) as allegedly unpatentable over Houser et al. (Cardiovascular Pathol 9(6): 317-322, 2000) in view of Kellner-Weibel et al. (Arterioscler Thromb Vasc Biol 18: 423-431, 1998). The Examiner alleged that it would have been obvious to one skilled in the art to substitute the U18666A for progesterone in the method of Houser et al. to achieve the predictable result of reducing aortic plaque load, inhibiting macrophage cell death, and inhibiting atherosclerotic lesional complications.

In response, applicant respectfully traverses the Examiner's ground of rejection. Nevertheless, without conceding the correctness of the Examiner's rejection, applicant notes that claims 1, 2 and 27 have been amended herein above and address the Examiner's comments as they were being applied to the amended claims.

Applicant's invention, as recited in amended claim 1, provides a method for inhibiting macrophage death in a subject having, or at increased risk for developing, cardiovascular disease which comprises administering to the subject an amount of an amphipathic amine or a pharmaceutically acceptable salt thereof effective to inhibit the intracellular transport of cholesterol within macrophage cells from an intracellular cholesterol storage site to the endoplasmic reticulum but not to the plasma membrane, so as to thereby inhibit macrophage death in the subject.

Applicant's invention further, as recited in amended claim 2, provides further a method for inhibiting atherosclerotic lesional complications in a subject having, or at increased risk for developing, cardiovascular disease which comprises administering to the subject an amount of an amphipathic amine or a pharmaceutically acceptable salt thereof effective to inhibit the intracellular transport of cholesterol within macrophage cells from an intracellular cholesterol storage site to the endoplasmic reticulum but not to the plasma membrane, so as to thereby inhibit atherosclerotic lesional complications in the subject.

Applicant's invention, as recited in amended claim 27, provides also a method for inhibiting atherosclerotic lesional necrosis or plaque rupture in a subject having, or at increased risk for developing, cardiovascular disease which comprises administering to the subject an amount of an amphipathic amine or a pharmaceutically acceptable salt thereof effective to inhibit the intracellular transport of cholesterol within macrophage cells from an intracellular cholesterol storage site to the endoplasmic reticulum but not to the plasma membrane, so as to thereby inhibit atherosclerotic lesional necrosis or plaque rupture in the subject.

In relying upon Houser et al. as the primary reference rendering applicant's claimed invention obvious the Examiner asserts that "the progesterone utilized in Houser et al. inherently performs the function required by the claims of the instant case..." The Examiner later refers to uncited prior art references Lange et al., Mazzone et al. and Aikawa et al.

The Examiner is incorrectly and improperly referring to what is inherently disclosed in Houser et al. Inherency can, in case where something necessarily occurs, be a basis for a rejection on the ground of lack of novelty. Inherency can never be a proper basis for an obviousness rejection. That which is not disclosed (i.e. only inherent) can never render something obvious.

The Examiner is also incorrectly and improperly referring to additional references which are not cited in the grounds for rejection.

Finally, the Examiner acknowledges that Houser et al. do not teach the administration of an amphipathic amine, i.e. the subject matter being claimed.

Thus, Houser et al. teaches none of the elements of applicant's claims and is not properly used as a primary reference in a rejection under 35 U.S.C. §103.

With respect to the secondary reference, Kellner-Weibel et al., the Examiner asserts that *in vitro* cotreatment with U18666A and ACAT inhibitor appeared to delay or suppress cell death but ignore the teaching in Kellner-Weibel that "the protective effect of U18666A was not due to a decrease in cellular FC concentrations because cells treated with an ACAT inhibitor accumulated similar amounts of FC in the presence or absence of U18666A" (See abstract).

Furthermore, Kellner-Weibel disclose on page 429 under "Cholesterol Efflux" that "further experiments would be required to establish whether pool(s) of excess cholesterol that induces cell death is exclusively in the plasma membrane". This statement to the extent relevant to the obviousness of applicant's claimed invention teaches to inhibit intracellular transport of cholesterol to the plasma membrane. In contrast, applicant's claimed invention is to inhibit intracellular transport of cholesterol to the endoplasmic reticulum but not to the plasma membrane. Clearly, applicant's invention so claimed is not obvious from the cited references.

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In view of these remarks, applicant maintains that claims 1, 2, 27 (as amended) and the claims which depend therefrom are not rendered obvious by Houser et al. in view of Kellner-Weibel et al. Accordingly, applicant respectfully requests the Examiner reconsider and withdraw this ground of rejection.

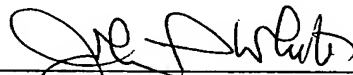
Conclusion

In view of the remarks hereinabove, applicant respectfully submits that the grounds of rejection set forth in the October 31, 2007 Office Action have been overcome. Applicant therefore respectfully requests that the Examiner reconsider and withdraw these grounds of rejection and allow claims as amended.

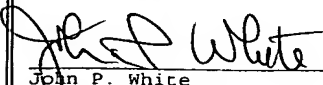
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed \$525.00 three-month extension fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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